

Applicants: Short and Keller  
Application No.: 09/848,651  
Filed: May 3, 2001  
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**In the Claims**

Please cancel claim 15 without prejudice.

Please amend claims 1, 4-8, and 13 and 15 as follows:

Bl-2  
1. (Currently Amended) A method of screening an environmental library for an agent that modulates ~~the~~ interaction of a first test protein linked to a DNA binding moiety and a second test protein linked to a transcriptional activation moiety, comprising

providing an environmental expression library containing a plurality of recombinant prokaryotic clones, wherein DNA for generating the library is naturally occurring and obtained from a mixed population of organisms;

co-encapsulating at least one of the prokaryotic clones with the first test protein and the second test protein in a suitable microenvironment; and

screening the microenvironment by fluorescence activated cell sorting (FACS) analysis to determine the ability of the an agent produced by the prokaryotic clone to modulate the interaction of the first test protein linked to a DNA binding moiety with the second test protein linked to a transcriptional activation moiety to produce a change in fluorescence of the microenvironment, wherein the change indicates the presence of the agent.

2. (Original) The method of claim 1, wherein the agent is an enzyme or small molecule.

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3. (Original) The method of claim 2, wherein the enzyme is selected from the group consisting of lipases, esterases, proteases, glycosidases, glycosyl transferases, phosphatases, kinases, mono- and dioxygenases, haloperoxidases, lignin peroxidases, diarylpropane peroxidases, epoxide hydrolases, nitrile hydratases, nitrilases, transaminases, amidases, and acylases.
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- B13 4. (Currently Amended) The method of claim 1, wherein the ~~agent inhibits the activity~~ modulation inhibits the expression of the first protein or the second protein.
5. (Currently Amended) The method of claim 1, wherein the ~~agent enhances the activity~~ modulation enhances the expression of the first protein or the second protein.
6. (Currently Amended) The method of claim 1, wherein the recombinant prokaryotic clone expressing the agent is ~~expressed from a recombinant cell~~ co-encapsulated with a second recombinant clone expressing a target fluorescent protein and detectable marker.
7. (Currently Amended) The method of claim 6, wherein the second recombinant clone is a eukaryotic cell.
8. (Currently Amended) The method of claim 6, wherein the second recombinant clone is a prokaryotic cell.
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9. (Original) The method of claim 1, wherein the microenvironment is a liposome, gel microdrop, bead, agarose, cell, ghost red blood cell or ghost macrophage.

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10. (Original) The method of claim 9, wherein the liposomes are prepared from one or more phospholipids, glycolipids, steroids, alkyl phosphates or fatty acid esters.
  11. (Original) The method of claim 10, wherein the phospholipids are selected from the group consisting of lecithin, sphingomyelin and dipalmitoyl.
  12. (Original) The method of claim 10, wherein the steroids are selected from the group consisting of cholesterol, chlorestanol and lanosterol.
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- B14
13. (Currently Amended) The method of claim 16, wherein the ~~detectable~~ fluorescent protein is a fluorescent dye, ~~a visible dye~~, a bioluminescent material, a chemiluminescent material, ~~a radioactive material~~, or ~~an~~ a fluorescent enzymatic substrate.
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14. (Original) The method of claim 13, wherein the bioluminescent material is green fluorescent protein (GFP) or red fluorescent protein (RFP).

15. Claim 15 (Cancelled)
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- B15
16. (New) The method of claim 1, wherein at least one test protein is derived from a mixed population of organisms
  17. (New) The method of claim 1, wherein the DNA for generating the library is normalized.
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